the other hand, directionality is an important observed effect leading to significant modification of the contrast response. This is especially important in the development of medical imaging contrast agents in general and most specifically with acoustic contrast agents.

The output from the boundary element model is used for the input of the propagation model as described below.

Microbubbles in solution undergo nonlinear radial oscillation when they are exposed to moderately strong (greater than 100 KPa) ultrasound waves. These oscillations produce echoes containing second and higher harmonics of the incident wave.

The pressure and the particle velocity in the coupled wave equations are the instantaneous total pressure and the total particle velocity at any point in the fluid medium. The equations for a lossless medium with variable speed and density are the following:

$$\nabla p(x,y,z,t) = -\rho(x,y,z,t)\, \partial u(x,y,z,t)/\partial t, \qquad (1)$$

$$\nabla u(x,y,z,t)=(-1/(\rho(x,y,z,t)c^2))\,(\partial p(x,y,z,t)/\partial t) \qquad (2)$$

The information needed to completely compute the different fields over time is the initial fields' distribution and the incident wave satisfying the two coupled equations. For the computation, the fields in the medium are set to zero at the initial time t=0. The two coupled equations are discretized to obtain the FDTD equations. The practical implementation of the FDTD method starts by partitioning the entire 3D space into small cubes following the Yee cell method. (Yee, "Numerical Solution of Initial Boundary Value Problems Involving Maxwell's Equations in Isotropic Media," *IEEE Trans. Antennas Prop.*, 14(8) 302-07 (1966)). Building a medium consists of labeling each cube so that a given scattering medium

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with specific material properties is obtained. The computational complexity of the problem is $O(n^3)$ and the storage requirement is also $O(n^3)$ where n is the number of cells on each side of a cubic geometry. The transducer is modeled as ideal point sources, generating a Gaussian spherical wave that propagates through the 3D medium. The architecture of the code is simple given the modular nature of each subroutine. Parallel processing can be used for larger medium simulation. The procedure for the simulations are: (1) generate the synthetic medium, (2) compute analytically the propagation of the incident field in the medium, and (3) compute the scattered pressure field and the scattered velocity field at each point in the medium.

The FDTD method can predict field disturbances due to short-range variations in medium density of the order of the wavelength of the incident wave. Applications for this method include the prediction of the acoustic field distribution in inhomogeneous media such as biological tissues, prediction of encapsulated microbubbles, insonification in different regimes, tissue characterization and blood flow. Synthetic media can be generated and used to compute the different scattered fields for analysis. Additionally, this method also can be used by first experimentally obtaining the medium parameters, i.e., by reconstruction, or from knowledge of anatomy of the given tissue, and then computing the various acoustic fields for specific studies.

EXAMPLES

The following examples are intended to illustrate the invention and not to limit or otherwise restrict the invention.

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Example 1 - Ultrasound Studies

Preliminary imaging studies were conducted to compare the cross-sectional ultrasound images of oil (containing no contrast agents), air-filled albumin microspheres, and unmodified and surface-modified GOAM flowing through a tube. An Aloka SSD5500 PHD ultrasound machine with a linear transducer (UST 5539 10 MHz) was used to create traditional B-mode ultrasound images. In these experiments, the above solutions were injected into clear plastic Tygon tubing (OD=0.318cm; ID=0.159cm) (Figure 4a) immersed in degassed water at room temperature. Cross-sectional images of the tube were captured using a personal computer, video frame grabber and real time video capture software (Capture©, Watkin, 1997). These images are shown in Figures 4b-4d.

These images clearly demonstrate the full circumference visualization capabilities of the various media – oil (no contrast media), air-filled albumin microspheres, and GOAM. Differences are clearly evident in the cross-sectional B-mode ultrasound images. The inner circumference of the tube is not visible when imaging with oil, which does not contain contrast media. Imaging with flowing (and static) air filled albumin microspheres enhances the tube image but the full circumference of the tube is not visible. GOAM provides full circumferential tube delineation and enhancement. This demonstrates the potential utility of modified GOAM for mapping of blood vessels, especially the delineation of small blood vessels. Modified GOAM has the potential to enhance visualization of flow in small vessels of the heart and perhaps enhance low velocity ultrasound spectral Doppler signals. Moreover, full vessel circumference imaging is an essential prerequisite to 3D imaging studies.

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